

CLAIMS

1. A nucleic acid which encodes a polypeptide consisting essentially of the amino acid sequences of SEQ ID Nos. 1 to 38 or a sequence complementary thereto.
2. The nucleic acid sequence according to claim 1, which encodes a polypeptide having at least 95% amino acid identity with the amino acid sequences of SEQ ID Nos. 1 to 38 or a sequence complementary thereto and retains the same binding affinity to said polypeptide of SEQ ID Nos. 1 to 38.
3. The nucleic acid according to claim 1, wherein said nucleic acid consists essentially of SEQ ID Nos 39 to 76 or a sequence complementary thereto.
4. The nucleic acid according to claim 3, wherein said nucleic acid has at least 95% nucleic acid identity with a nucleic acid of SEQ ID Nos. 39 to 76 or a sequence complementary thereto and retains the same binding affinity to said polypeptide of SEQ ID Nos. 1 to 38.
5. The nucleic acid according to claim 1, encoding a polypeptide having an amino acid sequence consisting essentially of:
 - 45 consecutive amino acids of SEQ ID No. 1;
 - 30 consecutive amino acids of SEQ ID No. 2;
 - 65 consecutive amino acids of SEQ ID No. 3;
 - 30 consecutive amino acids of SEQ ID No. 4;
 - 130 consecutive amino acids of SEQ ID No. 5;
 - 25 consecutive amino acids of SEQ ID No. 6;
 - 23 consecutive amino acids of SEQ ID No. 7;
 - 48 consecutive amino acids of SEQ ID No. 8;
 - 36 consecutive amino acids of SEQ ID No. 9;
 - 25 consecutive amino acids of SEQ ID No. 10;
 - 24 consecutive amino acids of SEQ ID No. 11;

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-37 consecutive amino acids of SEQ ID No. 12;
-25 consecutive amino acids of SEQ ID No. 13;
-30 consecutive amino acids of SEQ ID No. 14;
-27 consecutive amino acids of SEQ ID No. 15;
-69 consecutive amino acids of SEQ ID No. 16;
-130 consecutive amino acids of SEQ ID No. 17;
-33 consecutive amino acids of SEQ ID No. 18;
-25 consecutive amino acids of SEQ ID No. 19;
-40 consecutive amino acids of SEQ ID No. 20;
-78 consecutive amino acids of SEQ ID No. 21;
-39 consecutive amino acids of SEQ ID No. 22;
-57 consecutive amino acids of SEQ ID No. 23;
-26 consecutive amino acids of SEQ ID No. 24;
-68 consecutive amino acids of SEQ ID No. 25;
-34 consecutive amino acids of SEQ ID No. 26;
-42 consecutive amino acids of SEQ ID No. 27;
-48 consecutive amino acids of SEQ ID No. 28;
-102 consecutive amino acids of SEQ ID No. 29;
-49 consecutive amino acids of SEQ ID No. 30;
-92 consecutive amino acids of SEQ ID No. 31;
-49 consecutive amino acids of SEQ ID No. 32;
-55 consecutive amino acids of SEQ ID No. 33;
-69 consecutive amino acids of SEQ ID No. 34;
-23 consecutive amino acids of SEQ ID No. 35;
-33 consecutive amino acids of SEQ ID No. 36;
-32 consecutive amino acids of SEQ ID No. 37;
or
-22 consecutive amino acids of SEQ ID No. 38.

6. The nucleic acid according to claim 1 or claim 5, wherein said nucleic acid encodes a polypeptide having one to three amino acid substitutions, wherein said substitutions are made with equivalent amino acids.

7. A polypeptide consisting essentially of an amino acid sequence of SEQ ID Nos. 1 to 38 or a polypeptide having at least 95% amino acid identity with an amino acid sequence of SEQ ID Nos. 1 to 38 and retains the same binding affinity to said polypeptide of SEQ ID Nos. 1 to 38.

8. The polypeptide according to claim 7, wherein said polypeptide consists essentially of:

- 45 consecutive amino acids of SEQ ID No. 1;
- 30 consecutive amino acids of SEQ ID No. 2;
- 65 consecutive amino acids of SEQ ID No. 3;
- 30 consecutive amino acids of SEQ ID No. 4;
- 130 consecutive amino acids of SEQ ID No. 5;
- 25 consecutive amino acids of SEQ ID No. 6;
- 23 consecutive amino acids of SEQ ID No. 7;
- 48 consecutive amino acids of SEQ ID No. 8;
- 36 consecutive amino acids of SEQ ID No. 9;
- 25 consecutive amino acids of SEQ ID No. 10;
- 24 consecutive amino acids of SEQ ID No. 11;
- 37 consecutive amino acids of SEQ ID No. 12;
- 25 consecutive amino acids of SEQ ID No. 13;
- 30 consecutive amino acids of SEQ ID No. 14;
- 27 consecutive amino acids of SEQ ID No. 15;
- 69 consecutive amino acids of SEQ ID No. 16;
- 130 consecutive amino acids of SEQ ID No. 17;
- 33 consecutive amino acids of SEQ ID No. 18;
- 25 consecutive amino acids of SEQ ID No. 19;
- 40 consecutive amino acids of SEQ ID No. 20;
- 78 consecutive amino acids of SEQ ID No. 21;
- 39 consecutive amino acids of SEQ ID No. 22;
- 57 consecutive amino acids of SEQ ID No. 23;
- 26 consecutive amino acids of SEQ ID No. 24;
- 68 consecutive amino acids of SEQ ID No. 25;
- 34 consecutive amino acids of SEQ ID No. 26;

-42 consecutive amino acids of SEQ ID No. 27;
-48 consecutive amino acids of SEQ ID No. 28;
-102 consecutive amino acids of SEQ ID No. 29;
-49 consecutive amino acids of SEQ ID No. 30;
-92 consecutive amino acids of SEQ ID No. 31;
-49 consecutive amino acids of SEQ ID No. 32;
-55 consecutive amino acids of SEQ ID No. 33;
-69 consecutive amino acids of SEQ ID No. 34;
-23 consecutive amino acids of SEQ ID No. 35;
-33 consecutive amino acids of SEQ ID No. 36;
-32 consecutive amino acids of SEQ ID No. 37;
or
-22 consecutive amino acids of SEQ ID No. 38.

9. The polypeptide according to claim 7, wherein said polypeptide has from one to three amino acid substitutions, wherein said substitutions are made with equivalent amino acids.

10. The polypeptide according to claim 8, wherein said polypeptide has from one to three amino acid substitutions, wherein said substitutions are made with equivalent amino acids.

11. An antibody directed against a polypeptide according to claim 7 or claim 8.

12. A recombinant vector containing inserted therein a nucleic acid according to claim 1.

13. A recombinant vector containing inserted therein a nucleic acid according to claim 2.

14. A recombinant vector containing inserted therein a nucleic acid according to claim 3.

DRAFT - 1996

15. A recombinant vector containing inserted therein a nucleic acid according to claim 4.

16. A recombinant vector containing inserted therein a nucleic acid according to claim 5.

17. The recombinant vector according to any one of claims 12 to 16 which is a pACTII¹st plasmid or a pAS2 $\Delta\Delta$ plasmid.

18. The recombinant vector according to any one of claims 12 to 16, which is pT25, pKT25, pUT18 and pUT18C.

19. The recombinant vector according to any one of claims 12 to 16, which is pP6 and pB5.

20. A cell host transformed with a vector according to any one of claims 12 to 16.

21. A set of two nucleic acids consisting essentially of:

- (i) a first nucleic acid encoding a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10; and
- (ii) a second nucleic acid encoding a prey polypeptide which binds to the SID® polypeptide defined in i).

22. A set of two nucleic acids consisting essentially of the following:

SEQ ID No. 77/SEQ ID No.1; SEQ ID No. 78/SEQ ID No.2;
SEQ ID No. 78/SEQ ID No.3; SEQ ID No. 79/SEQ ID No.4; SEQ ID No. 80/SEQ
ID No.5; SEQ ID No. 81/SEQ ID No.6; SEQ ID No. 82/SEQ ID No.7; SEQ ID No.
83/SEQ ID No.8; SEQ ID No. 84/SEQ ID No.9; SEQ ID No. 85/SEQ ID No.10;

SEQ ID No. 86/SEQ ID No.11; SEQ ID No. 87/SEQ ID No.12; SEQ ID No. 88/SEQ ID No.13; SEQ ID No. 89/SEQ ID No.14; SEQ ID No. 90/SEQ ID No.15; SEQ ID No. 91/SEQ ID No.16; SEQ ID No. 92/SEQ ID No.17; SEQ ID No. 93/SEQ ID No.18; SEQ ID No. 94/SEQ ID No.19; SEQ ID No. 95/SEQ ID No.20; SEQ ID No. 96/SEQ ID No.21; SEQ ID No. 97/SEQ ID No.22 SEQ ID No. 98/SEQ ID No.23; SEQ ID No. 99/SEQ ID No.24; SEQ ID No. 100/SEQ ID No.25; SEQ ID No. 101/SEQ ID No.26; SEQ ID No. 102/SEQ ID No.27; SEQ ID No. 103/SEQ ID No.28; SEQ ID No. 104/SEQ ID No.29; SEQ ID No. 105/SEQ ID No.30; SEQ ID No. 106/SEQ ID No.31; SEQ ID No. 107/SEQ ID No.32; SEQ ID No. 108/SEQ ID No.33; SEQ ID No. 109/SEQ ID No.34; SEQ ID No. 110/SEQ ID No.35; SEQ ID No. 111/SEQ ID No.36; SEQ ID No. 112/SEQ ID No.37; or SEQ ID No. 113/SEQ ID No.38.

23. A set of two polypeptides consisting essentially of:

- i) a first polypeptide consisting essentially of a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10; and
- ii) a second prey polypeptide which binds specifically with the first polypeptide.

24. A set of two polypeptides consisting essentially of the following sets:

SEQ ID No. 114/SEQ ID No.39; SEQ ID No. 115/SEQ ID No.40; SEQ ID No. 115/SEQ ID No.41; SEQ ID No. 116/SEQ ID No.42; SEQ ID No. 117/SEQ ID No.43; SEQ ID No. 118/SEQ ID No.44; SEQ ID No. 119/SEQ ID No.45; SEQ ID No. 120/SEQ ID No.46; SEQ ID No. 121/SEQ ID No.47; SEQ ID No. 122/SEQ ID No.48; SEQ ID No. 123/SEQ ID No.49; SEQ ID No. 124/SEQ ID No.50; SEQ ID No. 125/SEQ ID No.51; No. 126/SEQ ID No.52; SEQ ID No. 127/SEQ ID No.53; SEQ ID No. 128/SEQ ID No.54; SEQ ID No. 129/SEQ ID No.55; SEQ ID No. 130/SEQ ID No.56; SEQ ID No. 131/SEQ ID No.57; SEQ ID No. 132/SEQ ID No.58; SEQ ID No. 133/SEQ ID No.59; SEQ ID No. 134/SEQ ID No.60; SEQ ID No. 135/SEQ ID No.61; SEQ ID No. 136/SEQ ID No.62; SEQ ID No. 137/SEQ ID No.63; SEQ ID No. 138/SEQ ID No.64; No. 139/SEQ ID No.65; SEQ ID No. 140/SEQ ID No.66; SEQ ID No. 141/SEQ ID No.67; SEQ ID No. 142/SEQ ID

No.68; SEQ ID No. 143/SEQ ID No.69; SEQ ID No. 144/SEQ ID No.70; SEQ ID No. 145/SEQ ID No.71; SEQ ID No. 146/SEQ ID No.72; SEQ ID No. 147/SEQ ID No.73; SEQ ID No. 148/SEQ ID No.74; SEQ ID No. 149SEQ ID No.75; or SEQ ID No. 150/SEQ ID No.76.

25. A complex formed between said set of two polypeptides of claim 23.

26. A complex formed between said set of two polypeptides of claim 24.

27. A method for selecting a molecule which inhibits the binding between a set of two polypeptides wherein said method comprises:

- a) cultivating a recombinant host cell containing a reporter gene the expression of which is toxic for said recombinant host cell, said host cell being transformed with two vectors wherein:
 - i) the first vector contains a nucleic acid comprising a polynucleotide encoding a first hybrid polypeptide containing one of said two polypeptides according to claim 23 and a DNA binding domain;
 - ii) the second vector contains a nucleic acid comprising a polynucleotide encoding a second hybrid polypeptide containing the second of said two polypeptides according to claim 23 and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;on a selective medium containing the molecule to be tested and allowing the growth of said recombinant host cell when the toxic reporter gene is not activated; and
- b) selecting the molecule which inhibits the growth of the recombinant host cell defined in step a).

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28. A method for selecting a molecule which inhibits the binding between a set of two polypeptides wherein said method comprises:

- c) cultivating a recombinant host cell containing a reporter gene the expression of which is toxic for said recombinant host cell, said host cell being transformed with two vectors wherein:
 - iii) the first vector contains a nucleic acid comprising a polynucleotide encoding a first hybrid polypeptide containing one of said two polypeptides according to claim 24 and a DNA binding domain;
 - iv) the second vector contains a nucleic acid comprising a polynucleotide encoding a second hybrid polypeptide containing the second of said two polypeptides according to claim 24 and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;
on a selective medium containing the molecule to be tested and allowing the growth of said recombinant host cell when the toxic reporter gene is not activated; and
- b) selecting the molecule which inhibits the growth of the recombinant host cell defined in step a).

29. A method for selecting a molecule which inhibits protein-protein interaction of a set of two polypeptides, wherein said method comprises the steps of:

- a.) cultivating a recombinant host cell containing a reporter gene the expression of which is toxic for said recombinant host cell, said host cell being transformed with two vectors wherein:
 - i) the first vector contains a nucleic acid comprising a polynucleotide encoding a first hybrid polypeptide

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containing one of said set of two polypeptides according to claim 23 and the first domain of an enzyme;

ii) the second vector contains a nucleic acid comprising a polynucleotide encoding a second hybrid polypeptide containing the second of said two polypeptides according to claim 23 and the second part of said enzyme capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting, said interaction recovering the catalytic activity of the enzyme; on a selective medium containing the molecule to be tested and allowing the growth of said recombinant host cell when the toxic gene is not activated; and

d) selecting the molecule which inhibits the growth of the recombinant host cell defined in step a).

30. A method for selecting a molecule which inhibits protein-protein interaction of a set of two polypeptides, wherein said method comprises the steps of:

a) cultivating a recombinant host cell containing a reporter gene the expression of which is toxic for said recombinant host cell, said host cell being transformed with two vectors wherein:

i) the first vector contains a nucleic acid comprising a polynucleotide encoding a first hybrid polypeptide containing one of said set of two polypeptides according to claim 24 and the first domain of an enzyme;

ii) the second vector contains a nucleic acid comprising a polynucleotide encoding a second hybrid polypeptide containing the second of said two polypeptides according to claim 24 and the second part of said enzyme capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting, said interaction recovering the catalytic activity of the enzyme;

on a selective medium containing the molecule to be tested and allowing the growth of said recombinant host cell when the toxic gene is not activated; and

- b) selecting the molecule which inhibits the growth of the recombinant host cell defined in step a).

31. A marker compound wherein said marker compound comprises:

- a.) a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10; and
- b.) a detectable molecule bound thereto.

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32. The marker compound of claim 31, wherein the detectable molecule is a fluorescent protein.

33. The marker compound of claim 32, wherein the detectable protein is a green fluorescent protein or a yellow fluorescent protein.

34. The marker compound of claim 31, wherein the detectable molecule has a catalytic activity.

35. The marker compound of claim 34, wherein the detectable molecule is a hydrolase, a transferase, a lyase, an isomerase, a ligase, a synthetase or a oxidoreductase.

36. The marker compound of claim 31, wherein the detectable molecule is a radioactive molecule.

37. The marker compound of claim 31, wherein the detectable molecule is chemiluminescent molecule.

38. The marker compound of claim 31, wherein the detectable molecule is covalently bound to said Selected Interacting Domain (SID®) polypeptide.

39. The marker compound of claim 31, wherein the detectable molecule is non covalently bound to the Selected Interacting Domain (SID®) polypeptide.

40. The marker compound of claim 31, wherein the detectable molecule is an antibody directed against the Selected Interacting Domain(SID®)polypeptide.

41. The marker compound of claim 40, wherein said antibody is labeled radioactively or nonradioactively.

42. The marker compound according to claim 31, wherein:

- a.) said Selected Interacting Domain (SID®) polypeptide is covalently bound to a first ligand; and
- b.) said detectable molecule comprises a second ligand which binds specifically to the first ligand.

43. The marker compound according to claim 42, wherein the first ligand is biotin and the second ligand is streptavidin.

44. A nucleic acid encoding a marker compound according to claim 42.

45. A recombinant vector comprising inserted therein a nucleic acid according to claim 44

46. The recombinant vector according to claim 45, which is pACTIIst , pASΔΔ, pT25, pKT25, pUT18, pUT18C, pP6 or pB5.

47. A recombinant host cell which has been transfected with said recombinant vector according to claim 45.

48. The recombinant host cell according to claim 45 which is of prokaryotic origin.

49. The recombinant host cell according to claim 45 which is of eukaryotic origin.

50. The recombinant host cell according to claim 49 which is a mammalian host cell.

51. A method of detecting a polypeptide of interest in a sample, said method comprising:

- a) contacting a marker compound or a plurality of marker compounds according to claim 31 with said sample; and
- b) detecting the complexes formed between said marker compound or plurality of marker compounds and said polypeptide of interest.

52. The method according to claim 51, wherein said marker compound is inserted in a recombinant vector.

53. The method according to claim 51, wherein said marker compound is in a recombinant host cell.

54. A method for detecting a polypeptide or a plurality of polypeptides of interest in a sample, wherein said method comprises:

- a) providing a substrate onto which a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10, or a plurality of Selected Interacting Domain (SID®) polypeptides according to any one of claims 7 to 10 is immobilized;
- b) bringing into contact the substrate defined in a) with the sample to be assayed;
- c) detecting the complexes formed between the Selected Interacting Domain (SID®) polypeptides or variants thereof or a variant thereof, or the plurality of Selected Interacting Domain (SID®) polypeptides and a molecule or a plurality of molecules initially contained in the sample.

55. The method of claim 54, wherein the Selected Interacting Domain (SID®) polypeptide or the plurality of Selected Interacting Domain (SID®) polypeptides are covalently bound to the substrate.

56. The method of claim 54, wherein the Selected Interacting Domain (SID®) polypeptide or the plurality of Selected Interacting Domain (SID®) polypeptides or variants thereof are non covalently bound to the substrate.

57. The method if claim 54, wherein the Selected Interacting Domain (SID®) polypeptide or the plurality of Selected Interacting Domain (SID®) polypeptides are covalently bound to a first ligand and wherein the substrate is coated with a second ligand which specifically binds to the first ligand.

58. The method of claim 57, wherein the first ligand is biotin and the second ligand is streptavidin.

59. The method according to claim 54, wherein the Selected Interacting Domain (SID®) polypeptide or a variant thereof, or the plurality of Selected Interacting Domain (SID®) polypeptides or variants thereof are covalently linked to a spacer and wherein said spacer is covalently bound to the substrate in order to immobilize the Selected Interacting Domain (SID®) polypeptide or a variant thereof, or the plurality of Selected Interacting Domain (SID®) polypeptides.

60. The method according to claim 54, wherein the detection step c) consists of detecting changes in the optical characteristics of the substrate.

61. A device for the detection of a polypeptide or a plurality of polypeptides of interest within a sample, said device comprises a substrate onto which a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10 or a plurality thereof is immobilized.

62. A pharmaceutical composition comprising a pharmaceutically effective amount of a nucleic acid comprising a polynucleotide encoding a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10.

63. A method for treating a viral infection by a Hepatitis C virus in a human or animal in need of such treatment, said method comprising administering to said human or said animal a pharmaceutically effective amount of a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10.

64. A method for treating a viral or a bacterial infection in a human or an animal in need of such treatment, said method comprising administering to said human or said animal a pharmaceutically effective amount of a recombinant expression vector comprising a polynucleotide encoding a Selected Interacting Domain (SID®) polypeptide according to any one of claims 7 to 10.

65. A method for selecting a Selected Interacting Domain (SID®) polypeptide comprising:

- 1) selecting a collection of nucleic acids (prey nucleic acids) which bind specifically to a given bait polypeptide of interest; and
- 2) determining the nucleic acid sequences which encode for a SID® polypeptide by:
 - a) selecting from the collection of prey nucleic acids obtained at the end of step 1) all prey nucleotides encoding a prey polypeptide capable of interacting with said bait polypeptide and containing a common nucleic acid fragment;
 - b) aligning the nucleotide sequences of the prey polynucleotides as selected at step a) and gathering in one set or in a plurality of sets of sequences those nucleotide sequences which have sequences that overlap for more than 30% of their respective nucleic acid length, wherein each common overlapping nucleotide sequence in one set of sequences defines a sequence encoding a pre-SID® polypeptide; and
 - c) aligning two sequences encoding two respective pre-SID® polypeptides; and:

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- i) defining an overlapping nucleic acid sequence between the sequences encoding the two respective pre-SID® polypeptides as a sequence encoding a SID® polypeptide, provided that the overlapping sequence is of at least 30 nucleotides in length;
- ii) defining a non-overlapping nucleic acid sequence between the sequences encoding the two respective pre-SID® polypeptides as a sequence encoding a SID® polypeptide, provided that (1) said non-overlapping sequence has more than 30 nucleotides in length and (2) said non-overlapping sequence represents at least 30% in length of any one of the polynucleotides contained in the set of prey polynucleotides used for defining the sequence encoding each pre-SID® polypeptide.

66. The method of claim 65, wherein said selection step 1) uses a yeast two-hybrid method or a bacterial two-hybrid method.

67. The method of claim 65, wherein step 2) further comprises the steps of:

- d) counting the number of overlapping prey polynucleotides contained in a first set of polynucleotides defining a sequence encoding a first SID® polypeptide;
- e) counting the number of overlapping prey polynucleotides contained in a second set of polynucleotides defining a sequence encoding a second SID® polypeptide which overlaps with the sequence encoding the first second SID® polypeptide;
- f) determining which sequence among those encoding respectively the first SID® polypeptide and the second SID® polypeptide has been defined with the largest number of prey polynucleotides and selecting this set of prey sequences;
- g) adding to the set of prey sequences selected at step f) those sequences that were contained in the set of prey sequences used for defining the sequence encoding the SID® polypeptide with the smallest number of prey sequences and which overlap with the sequence encoding the SID® polypeptide with the largest number of prey sequences;

- h) aligning the prey sequences added at step g) with the sequences already contained in the set of prey sequences which defined the sequence encoding the SID® polypeptide with the largest number of prey sequences; and
- i) defining an overlapping sequence between the whole sequences which were aligned in step h), wherein said overlapping sequence consists of a sequence encoding a SID® polypeptide.

68. The method according to Claim 65, wherein said SID® is from a virus.

69. The method according to claim 68, wherein the virus is a Hepatitis C virus.

70. The method according to claim 69, wherein the Hepatitis C virus is pathogenic for a mammal.

71. The method according to claim 70, wherein said mammal is a human.

72. A SID®nucleic acid selected according to the method of claim 65.

73. A SID® polypeptide encoded by a nucleic acid according to claim 72.

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10